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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	10/509,170
First Named Inventor	:	Nikolaos K. ROBAKIS
Filed	:	May 19, 2005
TC/A.U.	:	1654
Examiner	:	Roy R. Teller
Docket No.	:	102756.58236US
Customer No.	:	23911
Title	:	Peptides Derived from Cadherin and Methods of use Thereof

PETITION UNDER 37 CFR §1.181(a)
REQUESTING WITHDRAWAL OF
HOLDING OF ABANDONMENT

Mail Stop PETITION
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I hereby certify that this document is being deposited with the United States Postal Service as First Class Mail addressed to Mail Stop PETITION, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on this 14th day of October, 2008.

Julia K. Smith
(Signature)

Sir:

This Petition is in response to the Notice of Abandonment mailed on September 15, 2008 for the above-identified application.

The Notice of Abandonment states that the application is abandoned in view of Applicants' failure to timely file a reply to the Office letter mailed on March 6, 2008.

A reply to the Office letter was timely filed by first class United States Postal Service mail on September 8, 2008, with a petition for a three month extension of time and a credit card authorization in payment of the fee for the extension. The six month statutory deadline for responding to the Office letter was September 6, 2008, which was a Saturday. The response was filed on the next business day, September 8, 2008, and thus was timely filed. A copy of the response is submitted herewith.

The undersigned signed the Certificate of Mailing on the response filed September 8, 2008 and attests on a personal knowledge basis that the response was

deposited with the United States Postal Service as first class mail on September 8, 2008.

Accordingly, the reply was timely filed and Applicants respectfully petition for withdrawal of the holding of abandonment.

Applicants do not believe a fee is required by this communication. However, any fee necessitated by this communication may be charged to the Deposit Account of Crowell & Moring, LLP, Account Number 05-1323 (Docket # 102756.58236US).

Respectfully submitted,

October 14, 2008

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Title	:	Peptides Derived from Cadherin and Methods of use Thereof

AMENDMENT TRANSMITTAL

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I hereby certify that this document is being deposited with the United States Postal Service as First Class Mail addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on this 8th day of September, 2008.

Julia K. Smith
(Signature)

Sir:

Attached hereto are:

1. Amendment.
2. Supplemental Application Data Sheet.
3. Credit Card Payment Form (PTO-2038) in the amount of $525.00 for the three month extension of time fee.

Please credit any overpayment or charge any additional fees to the Deposit Account of Crowell & Moring, LLP, Account Number 05-1323 (Docket # 102756.58236US).

Respectfully submitted,

September 8, 2008

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Application No.	:	10/509,170
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Examiner	:	Roy R. Teller
Docket No.	:	102756.58236US
Customer No.	:	23911
Title	:	Peptides Derived from Cadherin and Methods of use Thereof

AMENDMENT

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I hereby certify that this document is being deposited with the United States Postal Service as First Class Mail addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on this 8th day of September, 2008.

Julia K. Smith
(Signature)

Sir:

This paper is in response to the Office Action mailed March 6, 2008 for the above-identified application. Applicants request a three-month extension of time for responding to the Office Action and enclose a Credit Card authorization in payment of the fee under 37 CFR §1.17(a)(3).

Amendments to the claims begin on page 2 of this paper.

Remarks begin on page 5 of this paper.

Amendments to the Claims

This listing of claims will replace all prior versions and listing of claims in this application.

Listing of Claims:

1. (Currently amended) A peptide ~~comprising~~ that binds to presenilin-1 and comprises the sequence EGGGE (SEQ ID NO: 5) wherein the peptide is from five to fifteen amino acids in length.

2. (Original) The peptide of Claim 1 comprising a sequence selected from the group consisting of EGGGEEDQDFDL (SEQ ID NO: 1), EGGGEMDTTSYD (SEQ ID NO: 2), EGGGEEDQDYDLS (SEQ ID NO: 3) and EGGGEED (SEQ ID NO: 4).

3. (Original) A composition comprising the peptide of Claim 1.

4. (Withdrawn) A method of inhibiting Presenilin-1-mediated γ-secretase activity comprising contacting a cell capable of exhibiting such activity with the composition of Claim 1.

5. (Withdrawn) A peptide comprising the sequence QPVEA (SEQ ID NO: 10) wherein the peptide is from five to fifteen amino acids in length.

6. (Withdrawn) The peptide of Claim 5 comprising the sequence KAQPVEAGLQI (SEQ ID NO: 9).

7. (Withdrawn) A composition comprising the peptide of Claim 5.

8. (Withdrawn) A method of inhibiting tumor metastasis comprising administering to a subject in need of such treatment a composition comprising a polypeptide or peptide comprising the matrix metalloproteinase cleavage site of cadherin or a functional equivalent thereof, in an amount effective to inhibit tumor metastasis.

9. (Withdrawn) The method of Claim 8 wherein the peptide comprises the sequence QPVEA (SEQ ID NO: 10).

10. (Withdrawn) A method of inhibiting apoptosis comprising contacting cells undergoing apoptosis with a composition comprising a polypeptide or peptide comprising the matrix metalloproteinase cleavage site of cadherin or a functional equivalent thereof, in an amount effective to inhibit apoptosis.

11. (Withdrawn) The method of Claim 10 wherein the peptide comprises the sequence QPVEA (SEQ ID NO: 10).

12. (Withdrawn) A method of determining susceptibility to Alzheimer's disease comprising measuring the intracellular domain cleavage product of cadherin in a cell from a subject, wherein a reduction in the cleavage product relative to the levels in control cells from a normal subject is indicative of susceptibility to Alzheimer's disease.

13. (Withdrawn) The method of Claim 12 wherein the intracellular domain cleavage product is selected from the group consisting of N-Cad/CTF2, E-Cad/CTF2 and VE-Cad/CTF2.

14. (Withdrawn) A method for identifying an agent that modifies presenilin-l-γ-secretase-like processing of cadherin comprising contacting a cell containing cadherin with a test compound; measuring production of the intracellular domain cleavage product of cadherin; and comparing production of the cleavage product in cells contacted with the test compound to production in cells not contacted with the test compound; wherein a difference in production of the cleavage product in the presence of the test compound is indicative of an agent that modifies-secretase-like processing of cadherin.

15. (Withdrawn) The method of Claim 14 wherein the intracellular domain cleavage product is selected from the group consisting of N-Cad/CTF2, E-Cad/CTF2 and VE-Cad/CTF2.

16. (Withdrawn) The method of Claim 14 wherein the cell is contained within a mammal.

17. (Withdrawn) A method for treating familial Alzheimer's disease comprising administering to a subject in need of such treatment a composition comprising an agent that increases the levels of the intracellular domain cleavage product of cadherin in the subject.

18. (Withdrawn) The method of Claim 17 wherein the agent is the intracellular domain cleavage product of cadherin.

19. (Withdrawn) The method of Claim 18 wherein the agent is selected from the group consisting of N-Cad/CTF2, E-Cad/CTF2 and VE-Cad/CTF2.

20. (Withdrawn) The method of Claim 17 wherein the agent is Presenilin 1.

21. (Withdrawn) A composition comprising the intracellular domain cleavage product of cadherin.

22. (Withdrawn) The composition of Claim 20 wherein the intracellular domain cleavage product of cadherin is selected from the group consisting of N-Cad/CTF2, E-Cad/CTF2 and VE- Cad/CTF2.

23. (Withdrawn) A method for treating familial Alzheimer's disease comprising administering to a subject in need of such treatment a composition comprising an agent that reduces CREB- mediated transcription.

REMARKS

In the Office Action mailed March 6, 2008, the Examiner has noted an error in the identification of the priority document. The correct priority application is 60/372,617 and the correct priority date is April 11, 2002. To correct an inadvertent typographical error in the Declaration and Power of Attorney, submitted herewith is a first-filed Application Data Sheet captioned "Supplemental Application Data Sheet."

Claims 1-3 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description in the specification. The Examiner has alleged that the claims are drawn to a genus of peptides, and that the number of disclosed species is insufficient to support the genus, and further that the specification does not provide relevant identifying characteristics of the genus.

Applicants respectfully disagree. The written description requirement for a genus may be satisfied by a description of a representative number of species, reduction to drawings, or by disclosure of relevant identifying characteristics sufficient to show the applicant was in possession of the claimed genus. "Guidelines for Examination of Patent Applications under 35 U.S.C. §112, paragraph 1, "Written Description" Requirements," Fed. Reg. 66(4)1103, II, A.3.a(2) ("the Written Description Guidelines"). See, also, Example 5 of the USPTO training materials regarding examination under the written description requirement for partial protein structure.

Claim 1 recites a genus of peptides from five to fifteen amino acids in length and comprising the sequence EGGGE. The specification discloses three representative species (SEQ ID NOS: 1, 2 and 3) at page 7, lines 4-7. The specification and claims describe the core conserved region of the peptide (EGGGE). The specification describes methods of deriving the peptides from E-cadherin, VE-

cadherin, and N-cadherin. Specification at page 6, line 19 – page 8, line 14. The specification further describes relevant identifying characteristics including function, i.e., ability to bind to presenilin-1, correlated with structure, i.e., the conserved region of the peptide (EGGGE). Specification at page 6, line 19 – page 7, line 14. Accordingly, the written description requirement has been satisfied.

In the interest of advancing prosecution, Claim 1 has been amended to recite the function of the peptide, i.e., "that binds to presenilin-1."

In view of the foregoing comments, withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Applicants note that the Office Action at page 6, first paragraph, refers to "antagonists of hedgehogs proteins" and assume that this paragraph was included in error. Clarification is requested.

Claims 1-3 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly vague and indefinite in the recitation "wherein the peptide is from 5 to 15 amino acids in length." The Examiner has alleged that when the peptide comprises the 12-mer of SEQ ID NO:1, it is unclear what the other three amino acids are. Claim 1 has been amended to recite that the peptide binds to presenilin-1. Accordingly, the claims are clear and definite to one of ordinary skill in the art, who can determine amino acids that may be included in a 15-mer peptide comprising SEQ ID NO:1 such that the peptide binds the presenilin-1. Accordingly, withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claims 1-3 have been rejected under 35 U.S.C. §103(a) as allegedly rendered obvious by U. S. Patent No. 6,787,136 to Brenner et al. ("Brenner et al."). The Examiner has alleged that Brenner et al. disclose a peptide having an amino acid sequence EEGGGEEDQD that reads on Claims 1 and 2.

Applicants respectfully disagree with the Examiner's characterization of the teaching of Brenner et al. Brenner et al. simply do not teach a peptide having the

amino acid sequence EEGGGEEDQD. Rather, the disclosure of Brenner et al. is directed to the molecular cloning of the gene encoding synovial cadherin. The cloning method included extraction and reverse transcription of mRNA from rheumatoid synoviocytes, followed by PCR amplification of the resulting template. The PCR primers were designed by aligning the amino acid sequences of E-, P-, and N-cadherin and observing regions of identity. Four regions of identity were appreciated, including a region corresponding to human E-cadherin residues 753-762 (EEGGGEEDQD). Degenerate oligonucleotide primers were designed based upon these regions of identity. These steps were performed by examining strings of letters on paper or by computer. No peptides are isolated or synthesized, nor do Brenner et al. suggest making a peptide having a specific sequence. Further, Brenner et al. do not attribute any function or utility to any region of the sequence. Brenner et al. merely identify a region of a sequence by a sequence identification number; a peptide having that sequence is neither taught nor suggested.

The Examiner has further alleged that Brenner et al. disclose the amino acid sequence of a human cadherin-11 protein, and further discloses that unique fragments are those that retain a distinct functional capability of the polypeptide, and that a unique fragment will depend upon whether the fragment constitutes a portion of a conserved domain. Thus it would have been obvious to prepare the instantly claimed peptides, the Examiner has alleged.

Applicants disagree. Brenner et al. do not teach <u>any</u> specific peptides from the sequence of human cadherin-11, no less the peptides claimed herein that bind presenilin-1. Rather, Brenner et al. include vague, general language directed to so-called unique fragments of a 796 amino acid polypeptide. In particular, at Column 13, lines 8-10, Brenner et al. state that "[v]irtually any segment of SEQ ID NO:2 that is nine or more amino acids in length and which is not common to other distinct polypeptides will be unique." Brenner et al. thus contemplate hundreds of

thousands of fragments and provide no direction as to any particular fragment, nor any indication as to function of any fragment.

Further, Brenner et al. do not teach that a unique fragment of a cadherin-11 polypeptide will depend upon factors such as whether the fragment constitutes a portion of a conserved protein domain, as the Examiner has alleged. Rather, as discussed above, the reference teaches that virtually any segment of 9 or more amino acids is contemplated, and that the size of the fragment will depend upon factors such as whether the fragment constitutes a portion of a conserved protein domain. Brenner et al. at Column 12, line 67 – Column 13, line 3.

Accordingly, there is no rationale to motivate an ordinary skilled artisan to make the peptides of the claimed invention and no expectation of success in achieving the claimed peptides. A prima facie case of obviousness thus has not been established. Withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

In view of the foregoing comments and amendments, it is respectfully submitted that the present application is in condition for allowance. Favorable reconsideration and allowance of all pending claims is requested.

Respectfully submitted,

September 8, 2008

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SUPPLEMENTAL APPLICATION DATA SHEET

APPLICATION INFORMATION

Application Number:	10/509,170
Filing Date:	May 19, 2005
Application type:	Nonprovisional
Subject Matter:	Utility
Title:	PEPTIDES DERIVED FROM CADHERIN AND METHODS OF USE THEREOF
Attorney Docket No.:	102756.58236US
Request for Early Publication:	No
Request for Non-Publication:	No
Suggested Drawing Figure:	
Total Drawing Sheets:	20
Small Entity:	Yes
Petition included:	No

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REPRESENTATIVE INFORMATION

Representative customer number: 23911

DOMESTIC PRIORITY INFORMATION

Application:	Continuity Type:	Parent Application:	Parent Filing Date:
	371 of International	**PCT/US03/11359**	**April 10, 2003**
PCT/US03/11359	**Nonprovisional**	**60/372,617**	**April 11, 2002**

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